Applicants: Wei Gu et al. Docket No.19240.431-US1

Application No.: 10/813,177 Filed: March 29, 2004

Amendments to the Claims

1 - 46. (canceled)

- 47. (previously presented) A method for determining whether an agent modulates a Mdm2-herpesvirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps of:
 - (a) obtaining or generating an in vitro system comprising Mdm2 and HAUSP;
 - (b) contacting the in vitro system with a candidate agent; and
- (c) determining whether the candidate agent increases or decreases a level of Mdm2-HAUSP protein complex in the *in vitro* system,

wherein determination of an increase or decrease the level of Mdm2-HAUSP protein complex in (c) indicates that the agent modulates Mdm2-HAUSP interaction.

48. (previously presented) The method of claim 47, wherein the determining in step (c) comprises comparing the level of Mdm2-herpesvirus-associated ubiquitin-specific protease (HAUSP) protein complex in the *in vitro* system of step (b) with a level of Mdm2-HAUSP protein complex in a second *in vitro* system comprising Mdm2 and HAUSP in the absence of the candidate agent, wherein determination of an increase or decrease of the level of Mdm2-HAUSP protein complex in the *in vitro* system of step (b) compared to the second *in vitro* system indicates that the agent modulates Mdm2-HAUSP interaction.

49 - 53. (canceled)

- 54. (presently amended) A method for determining whether an agent is reactive with Mdm2 or herpesvirus-associated ubiquitin-specific protease (HAUSP), comprising the steps of
- (a) contacting a candidate agent with either(i) Mdm2, in the presence of <a href="hereaverup-either-eith

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(b) determining whether the candidate agent inhibits Mdm2-HAUSP protein complex formation.

wherein determination of inhibition of Mdm2-HAUSP protein complex formation in (b) compared to Mdm2-HAUSP protein complex formation in the absence of the agent indicates that the agent is reactive with Mdm2 or HAUSP.

55 - 61. (canceled)

- 62. (presently amended) A method for determining whether an agent modulates Mdm2herpesyirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps of:
- (a) obtaining or generating a first in vitro system comprising Mdm2 and HAUSP, and a second in vitro system comprising Mdm2 and HAUSP;
 - (b) contacting the first system with a candidate agent:
- (c) contacting the second system with (i) the candidate agent and (ii) an antibody, or fragment thereof, that specifically binds Mdm2; and
- [[(c)]] (d) determining a level of HAUSP activity in the first system and the second system,

wherein determination of an increase or decrease of HAUSP activity in the first system compared to the second system indicates that the agent modulates Mdm2-HAUSP interaction.

- 63. (presently amended) A method for determining whether an agent modulates Mdm2herpesvirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps of:
- (a) obtaining or generating a first in vitro system comprising Mdm2 and HAUSP, and a second in vitro system comprising Mdm2 and HAUSP;
 - (b) contacting the first system with a candidate agent;

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(c) contacting the second system with (i) the candidate agent and (ii) an antibody, or fragment thereof, that specifically binds HAUSP; and

[[(c)]] (d) determining a level of Mdm2 activity in the first system and the second system.

wherein determination of an increase or decrease of Mdm2 activity in the first system compared to the second system indicates that the agent modulates Mdm2-HAUSP interaction.

- 64. (presently amended) The method of claim 54 or 57, further comprising the steps of:
- (c) contacting a cell with the candidate agent, wherein the cell comprises Mdm2, herpesvirus-associated ubiquitin-specific protease (HAUSP), or p53; and
- (d) determining whether the agent activates or increases, or inhibits or decreases, one or more Mdm2-associated, HAUSP-associated, or p53-associated biological events in the cell, compared to a cell not contacted with the candidate agent.